US Army Medical Research and Materiel

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Overcoming Interference in Alphavirus Immune Individuals

Features and advantages:

- V3526 vaccination of mice results in protective immunity against VEE
- V3526 vaccine-induced VEE immunity is not adversely affected by prior EEE vaccination
- Alphavirus replicon vaccine- induced immunity is not adversely affected by prior EEE vaccination

This invention provides a composition and a method for overcoming alphavirus vaccine interference. It includes a new Venezuelan equine encephalitis (VEE) vaccine candidate, V3526, which was developed using site-directed mutagenesis to incorporate desired mutations into a full-length infectious clone and alphavirus replicon-vectored vaccines. Studies using the method provide evidence that alphavirus interference is caused by the binding of interfering antibodies to viral epitopes which are accessible on infected cells but not on unbound virions.

The alphaviruses cause Venezuelan, western, and eastern equine encephalitis (VEE, WEE and EEE, respectively) and other, similar diseases in humans and horses. Symptoms include fever, headache, photophobia and seizures. Since immunity to one alphavirus does not adequately protect against subsequent exposure to other virulent, heterologous alphaviruses, a vaccine is needed that can overcome interference. In horses, for example, prior immunity to EEE or WEE viruses interferes with the induction of protective immune responses that would be expected after vaccination with the current VEE vaccine, TC-83.

V3526 contains a cleavage site deletion in a precursor glycoprotein sequence and a viability-restoring mutation at a another glycoprotein sequence. The mutations result in [illegible] that has glycoprotein spikes containing an additional protein (E3). The mutations may alter the sequence, conformation and/or accessibility of cross-reactive epitopes such that cross-reactive antibodies can no longer bind the glycoproteins during viral replication. In the presence of binding by interfering antibodies, V3526 should induce similar neutralizing antibody titers in both naïve and alphavirus immune recipients, thus overcoming vaccine interference.

Patent Status

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